REMARKS

Claims 1, 4, 6-9, 11-16 and 31 are pending. No new matter has been added by way of the present submission. For instance, claims 1 and 9 have been amended to include the phrase "*in vitro*" after "An animal cell." Further, the phrase "both of" has been inserted before "the following polynucleotides (a) and (b)" in various claims in order to more clearly define the phrase "a DNA comprising in a molecule, the following polynucleotides (a) and (b)." Also, claims 1, 9 and 14 include amendments to polynucleotide (a) wherein it is recited that it comprises a reporter protein coding region connected "functionally" downstream from a transcription control region as illustratively supported by page 18, lines 23-27 of the substitute specification. Further, the transcription control region of polynucleotide (a) in claims 1, 9 and 14 is amended to require that it "contains no functional elements relating to transcription control in said cell other than the recognition sequence and the minimum promoter" as illustratively supported by page 18, lines 9-18 of the substitute specification. Also, claims 1, 9 and 14 have been amended to include subject matter taken from claim 30, now cancelled. Lastly, claims 1, 11, 12, 14 and 31 have been amended to more clearly recite certain limitations in the alternative. Accordingly, no new matter has been added.

In view of the following remarks, Applicants respectfully request that the Examiner withdraw all rejections and allow the currently pending claims.

Issue under 35 U.S.C. § 101

The Examiner has rejected claims 1, 4 and 6-9 under 35 U.S.C. § 101 asserting that these claims read upon "*in vivo*" human tissue and are therefore non-statutory. Applicants submit that

independent claims 1 and 9 have been amended to include the phrase "*in vitro*" after "An animal cell." Therefore, the rejected claims do not read on a part of a living human *in situ*. This rejection is therefore moot. Reconsideration and withdrawal thereof are respectfully requested.

Issues under 35 U.S.C. § 112, first paragraph

The Examiner has rejected claims 1, 4, 6-9 and 11-16 under 35 U.S.C. § 112, first paragraph, for the reasons recited at pages 3-12 of the outstanding Office Action. The Examiner has provided grounds of rejection based upon enablement (see pages 3-9) and written description (see pages 9-12). Applicants respectfully traverse these rejections.

Enablement and Written description requirement

Applicants respectfully submit that the present specification provides detailed information of nucleic acid molecules and cells encompassed by the pending claims, for example, regarding a ligand-responsive transcription control factor selected from among an aryl hydrocarbon receptor, estrogen receptor, androgen receptor and thyroid hormone receptor, recognition sequences of the ligand-responsive transcription control factors, polynucleotides encoding reporter proteins, a minimum promoter comprising the nucleotide sequence of SEQ ID NO: 5, polynucleotides encoding selective marker proteins, and host animal cells with specific examples, the sequence identified in the sequence listing, and methods for obtaining those molecules and cells.

To more clearly reflect the present invention, certain amendments have been made to the claims as already discussed above. For instance, in claims 1, 9 and 14, polynucleotide (a) is

recited as comprising a reporter protein coding region connected functionally downstream from a transcription control region. Also, in claims 1, 9 and 14, the transcription control region in polynucleotide (a) is recited that it contains no functional elements relating to transcription control in said cell other than the recognition sequence and the minimum promoter. Further, claims 1, 9 and 14 have been amended to include subject matter taken from non-rejected claim 30. Lastly, in claims 1, 9 and 14, the phrase "both of" has been inserted before "the following polynucleotides (a) and (b)" in order to define the phrase "a DNA comprising in a molecule, the following polynucleotides (a) and (b)" more precisely.

In view of the above, Applicants submit that the pending claims fully satisfy the requirements of 35 U.S.C. § 112, first paragraph.

Additionally, the Examiner has mentioned at page 7 of the Office Action that the specification provides only one example of luciferase reporter assay using T3 as the chemical substance on a HeLa cell comprising plasmid pGL3-TATA-TREx5-BSD in a thyroid hormone receptor. However, Applicants point out that in fact, the specification provides plural examples of luciferase reporter assay using other cells, such as:

luciferase reporter assay using 17β estradiol as the chemical substance on a NIH3T3 cell comprising plasmid pGL3-TATA-EREx5-BSD in a estrogen receptor α (Example 4),

luciferase reporter assay using 3-methylcholanthrene as the chemical substance on a MCF7 cell comprising plasmid pGL3-TATA-1A1-BSD in an aryl hydrocarbon receptor (Example 5),

luciferase reporter assay using genistein as the chemical substance on a NIH3T3 cell comprising plasmid pGL3-TATA-EREx5-BSD in a estrogen receptor α (Test Example 1),

luciferase reporter assay using 17β estradiol as the chemical substance on a NIH3T3 cell comprising plasmid pGL3-TATA-EREx5-BSD in a estrogen receptor β (Example 9 and Test Example 2),

luciferase reporter assay using dihydrotestosterone as the chemical substance on a HeLa cell comprising plasmid pGL3-TATA-MMTV-BSD in an androgen receptor (Example 12),

luciferase reporter assay using T3 as the chemical substance on a HeLa cell comprising plasmid pGL3-TATA-TREx5-BSD in a thyroid hormone receptor α (Example 15 and Test Example 4), and

luciferase reporter assay using T3 as the chemical substance on a HeLa cell comprising plasmid pGL3-TATA-TREx5-BSD in a thyroid hormone receptor β (Example 15 and Test Example 4).

It is therefore clear that those of skill in the art would understand that Applicants were in possession of the claimed invention at the time of filing. Also, those of skill in the art are fully able to make and use the claimed invention without undue experimentation. The Examiner is therefore respectfully requested to withdraw these rejections.

Issue with respect to alleged "new matter"

The Examiner has also rejected claims 1, 4, 6-9, 11-16, 30 and 31 under 35 U.S.C. § 112, first paragraph, ("new matter") for the reasons recited at pages 12-13 of the outstanding Office Action. Applicants respectfully traverse this rejection.

Applicants respectfully submit that the present specification discloses the molecular biology steps taken to construct a polynucleotide comprising the nucleotide sequence of SEQ ID NO: 5 in detail.

As described in Example 1(1), two oligonucleotides,

5'-GATCTCGACTATAAAGAGGGCAGGCTGTCCTCAAGCGTCACCACGACTTCA-3'

(SEQ ID NO: 5) and

5'-AGCTTGAAGTCGTGGTGACGCTTAGAGGACAGCCTGCCCTCTTTATAGTCGA-3'

(SEQ ID NO: 6)

composed of nucleotide sequences derived from a nucleotide sequence near the TATA box of a mouse metallothionein I gene and the leader sequence (Genbank Accession No. J00605), were annealed to obtain a double stranded DNA, and T4 polynucleotide kinase was allowed to act thereon to phosphorylate the both ends thereof (hereinafter, this DNA is referred to as TATA DNA).

A plasmid pGL3 (manufactured by Promega) containing a fire fly luciferase gene was digested with restriction enzymes Bgl II and Hind III, to this was further added Bacterial alkaline phosphatase (BAP) and the mixture was kept at 65°C for 1 hour. Then, this incubated solution was subjected to electrophoresis using an agarose having a low melting point (Agarose L; manufactured by Nippon Gene) to recover DNA showing an electrophoretic movement corresponding to the length of the Bgl II-Hind III fragment containing a luciferase gene derived from pGL3. About 100 ng of this DNA and 1 μg of the above-mentioned TATA DNA were

mixed and bonded via a T4 ligase to produce a plasmid pGL3-TATA. Figures and literature references regarding TATA DNA and pGL3 are attached hereto.

Plasmid pGL3-TATA comprises the nucleotide sequence of SEQ ID NO: 5, as shown below. Each nucleotide sequence of SEQ ID NO: 18, used to construct pGL3-TATA in Example 10, and SEQ ID NO: 25, used to construct pGL3-TATA in Example 13, is identical to the nucleotide sequence of SEQ ID NO: 5; and each nucleotide sequence of SEQ ID NO: 19, used to construct pGL3-TATA in Example 10, and SEQ ID NO: 26, used to construct pGL3-TATA in Example 13, is identical to the nucleotide sequence of SEQ ID NO: 6.

Plasmid pGL3-TATA was used to construct plasmid pGL3-TATA-1A1-BSD, pGL3-TATA-EREx5-BSD, pGL3-TATA-MMTV-BSD and pGL3-TATA-TREx5-BSD.

It is therefore evident that there exists explicit support in the disclosure for a cell comprising a polynucleotide comprising a minimum promoter comprising the nucleotide sequence of SEQ ID NO: 5. The Examiner is therefore respectfully requested to withdraw this rejection.

In summary, Applicants submit that the present claims satisfy all statutory requirements for patentability. Accordingly, the Examiner is respectfully to withdraw all rejections and allow the currently pending claims.

If the Examiner has any questions or comments, please contact Craig A. McRobbie, Registration No. 42, 874 at the offices Birch, Stewart, Kolasch & Birch, LLP.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37.C.F.R. §§1.16 or 1.14; particularly, extension of time fees.

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Respectfully submitted,

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Attachments: Figures and literature references regarding TATA DNA and pGL3.